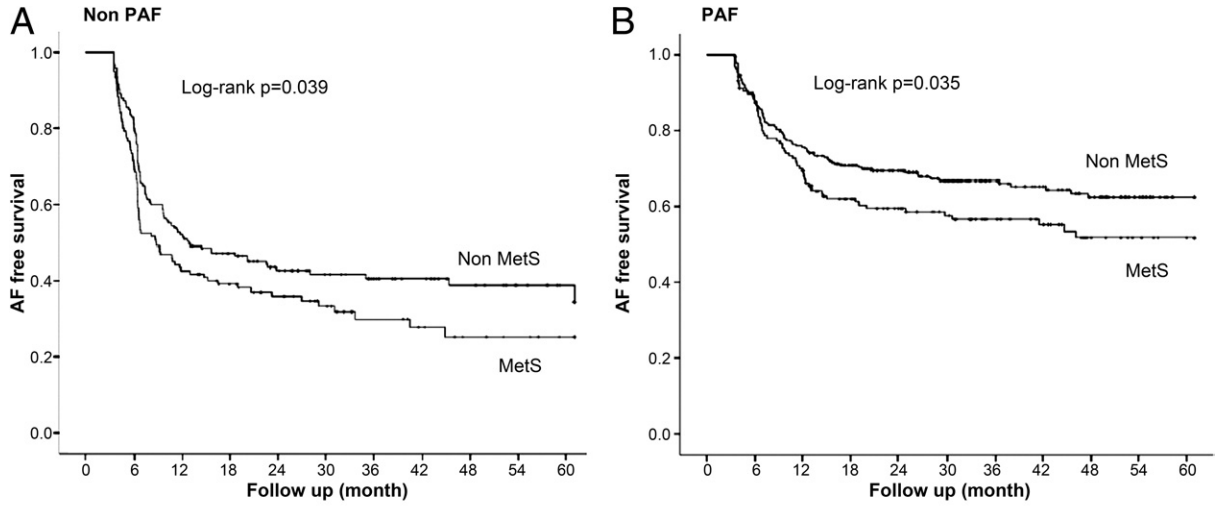

	n=702	Total	Events	Censored N	Censored %
PAF	Non MetS	261	88	173	66,3%
	MetS	156	67	89	57,1%
	Total	417	155	262	62,8%
Non PAF	Non MetS	165	97	68	41,2%
	MetS	120	82	38	31,7%
	Total	285	179	106	37,2%
Total	Total	702	334	368	52,4%

Figure 1 **Kaplan-Meier Curves**

Kaplan-Meier curves showing the probability of survival free from atrial fibrillation (AF) or atrial tachycardia after the first procedure in patients with **(A)** nonparoxysmal (Non PAF) and **(B)** paroxysmal atrial fibrillation (PAF). MetS = metabolic syndrome; Non MetS = patients without metabolic syndrome.

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Reply

We thank Dr. Wojcik and colleagues for their interest in our study (1).

The apparent contradiction between our findings and their results can be explained by at least 3 factors: difference in study population, detection and elimination of nonpulmonary vein (non-PV) triggers, and use of discretion of the physician in patient selection.

Our population had predominantly nonparoxysmal atrial fibrillation (NPAF), compared with theirs. Most importantly, we observed in the NPAF cohort significantly more frequent non-PV triggers in the metabolic syndrome (MS) group compared with the non-MS group, which is in accordance with earlier studies by others (2). As we discussed in our study, the challenge of eliminating non-PV triggers could have contributed to the higher recurrence in the MS group of the NPAF cohort. Of note,

Berkowitsch et al. (3) did not find any association between MS and non-PV triggers. This is likely because they did not perform any provocative test or pharmacological challenge to disclose non-PV triggers (which we routinely do) and missed a crucial piece of information that limited their approach to pulmonary vein isolation alone. Besides that, their study design allowed physician discretion in selecting radiofrequency versus cryoballoon ablation. The consequent radiofrequency cohort might have been different from ours.

Dr. Wojcik and colleagues raise question on the homogeneity of the study groups in terms of left atrium size (LAS). We agree that the propensity score matching is important in reducing bias. However, this involves the assumption of conditional independence (i.e., selection bias is eliminated by controlling for differences in observables). We are not certain whether that assumption is true about LAS in the context of MS. Indeed, left atrial dilation has been proposed to be a possible mechanism for the occurrence of atrial fibrillation (AF) in patients with MS (3). Furthermore, many elements of MS are known to be related to increased LAS. Therefore, we consider left atrial dilation as one of the mechanisms of how MS affects the outcome and not a confounder.

With regard to the possible confounding effects of use of renin-angiotensin-aldosterone blockers and statins in patients with and without MS, it can be safely said that the claimed benefit of these upstream drugs in preventing post-ablation AF recurrences is not supported by strong clinical evidence. A recent randomized trial clearly showed no effect of atorvastatin in preventing post-ablation AF recurrences (5), and the randomized trials specifically designed to evaluate the effect of renin-angiotensin-aldosterone blockers on AF recurrence reported negative results (5).

Finally, we acknowledge that longer follow-up would provide better insight into this association.

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